
Sex or Gender Reporting in Ophthalmology Clinical Trials Among United States Food and Drug Administration Approvals Between 1995-2022

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Introduction: As critical determinants of scientific rigor, reproducibility, and equity, sex and gender should be considered in clinical trial design and reporting. This study aimed to evaluate the accuracy of sex and gender reporting and extent of sex- and gender-based analysis in clinical trials associated with United States Food and Drug Administration (FDA) drug approvals between January 1, 1995 and December 31, 2022.

Methods: Design, Setting, and Participants: In this cross-sectional study, the following trial documents were reviewed by pairs of independent reviewers in decreasing order of priority: peer-reviewed publication, ClinicalTrials.gov report, and FDA medical and statistical reviews. Trial protocols and supplementary materials were also reviewed.

Main Outcome Measures: The proportion of trials that correctly applied sex and gender terminology, reported the method of assessing sex or gender, and conducted sex- or gender-based data analysis. Incorrect application of sex and gender terminology was defined as interchangeable use of sex- and gender-related terms without a clear justification.

Results: Between 1995-2022, 34 ophthalmic drugs corresponding to 85 trials received FDA approval, of which 16 drugs (47.1%) corresponding to 32 trials (37.6%) were associated with peer-reviewed publications. Sixteen (19.5%) trials used sex and gender terminology correctly. No trial reported how sex and gender were collected nor enrolled participants from sexual orientation and gender identity minority populations. Most trials (96.5%) reported sex- and gender-disaggregated demographic data, but few conducted sex- or gender-based analysis for data on dropout (1.2%), primary outcomes (28.2%), secondary outcomes (2.4%), and adverse events (9.4%). Erroneous sex and gender reporting was associated with later publication year (2008.5 vs. 2001.0; median difference, 7.5; 95% CI, -6.0 to 11.0; $P<.001$) and higher journal influence metrics, including 2022 journal impact factor (13.7 vs. 5.9; median difference, 7.8; 95% CI, -1.4 to 152.4, $P<.001$) and 2022 journal citation indicator (4.9 vs. 2.1; median difference, 2.9; 95% CI, 0 to 20.0, $P<.001$).

Conclusion: Over three-quarters of ophthalmology trials associated with FDA drug approvals conflate sex and gender and over two-thirds lack sex- and gender-based analyses. More rigorous integration of sex and gender appears warranted for FDA and presumably other trials to improve their validity, reproducibility, and equity.